

The Isolation of Farnesyl Acetone from Cigar Smoke Condensate

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Methyl ketones that appear to be derived from terpene precursors have recently been isolated from tobacco leaf and smoke. Johnson and Nicholson (4) have isolated solanone (II), an unsaturated ketone, from cigarette leaf. More recently, Cook and Rodgman (2) have isolated hexahydrofarnesyl acetone (III), a saturated eighteen carbon methyl

ketone having a partial isoprenoid structure, from cigarette smoke. We now wish to report the presence of farnesyl acetone (I), 6,10,14-trimethyl-5,9,13-pentadecatriene-2-one,

from a neutral fraction (also containing hydrocinnamyl nitrile, 3,5-dimethylphenol, a methylethylphenol, solanone and phytol (7)) of cigar smoke condensate.

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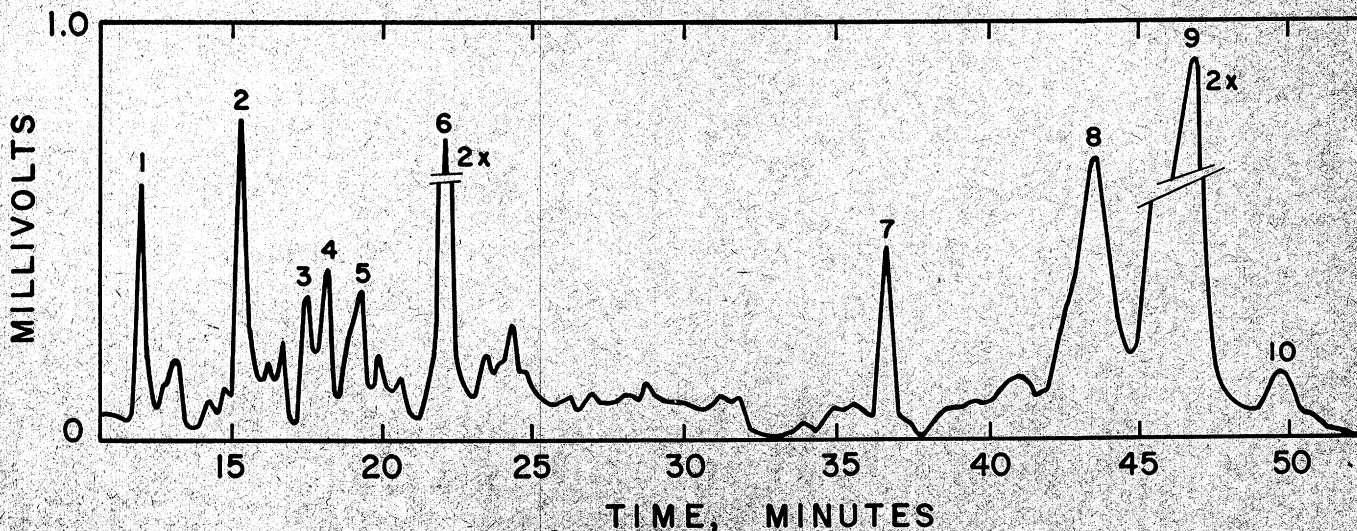
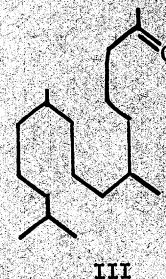
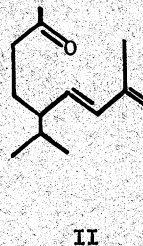
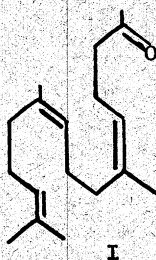


Figure 1.—Chromatogram of neutral fraction containing farnesyl acetone (peak 7).

The neutral fraction of cigar smoke condensate was subjected to chromatography on silicic acid. A fraction eluting with benzene was shown to contain at least twenty compounds when investigated by gas chromatography (Figure 1). The eluate corresponding to peak 7 was collected for further investigation.

Infrared analysis indicated that the compound was an unsaturated methyl ketone. There was no appreciable ultraviolet absorption above 220 m μ . The mass spectrum showed a parent peak at mass 262. The formula consistent with this molecular weight is C₁₈H₃₀O (assuming one oxygen atom in the molecule). A compound of this formula must contain four degrees of unsaturation (one of them being the carbonyl unsaturation). The mass spectrum was also consistent with the fact that the compound was a methyl ketone. The NMR spectrum contained a singlet at 8.3 τ (allylic methyl hydrogens), another singlet at 7.9 τ (hydrogens on methyl group α to carbonyl) and a poorly resolved peak at 5.0 τ (vinyl hydrogens). The ratio of vinyl hydrogens to hydrogen on methyl groups α to a vinyl group was approximately 1:4. Microhydrogenation (6) of the unknown compound with Pd/charcoal in ethanol indicated that the remaining three degrees of unsaturation were olefinic double bonds. The reduced product was isolated and readily identified by comparison of its mass spectrum, gas chromatographic behavior and infrared and ultraviolet data with hexahydrofarnesyl acetone synthesized from phytol (1). The carbon skeleton was therefore established and only the position of the double bonds remained to be determined. There are four possible structures consistent with the UV, IR and NMR data (I, IV-VI). A *priori* structure I

This compound was synthesized from nerolidol and ethyl acetoacetate according to the method described by Nazarov *et al.* (5). Actually this synthesis yielded two products that could be distinguished by gas chromatography. One of these compounds (the configuration was not established) which was identical to the compound isolated from the smoke by comparison of infrared, ultraviolet and mass spectra as well as gas chromatographic behavior gave a semicarbazone derivative (M.P. 76-78°C) consistent with farnesyl acetone (3).

Compound I was also isolated by a second method in order to show it was not produced as an artifact of the original isolation procedure. This alternative method (see Experimental) avoided strong acid or base treatment; we also tried to minimize other factors that might be responsible for the formation of artifacts.

We could not obtain data as to the amounts of this compound in the smoke condensate because of its relatively small concentration.

To our knowledge, this is the first report in the literature of the isolation of this compound from a natural product although it has been synthesized as an intermediate in the synthesis of vitamin K (3). We have been able to isolate this compound from cigarette smoke condensate as well as from the condensate of four different types of cigars; however, we have not attempted to isolate this compound from tobacco leaf directly.

Experimental

Isolation of farnesyl acetone:

a. The acids and bases were removed from an ether solution of the smoke condensate from 1500 commercial cigars by the usual method (8). The ether solution was concen-

trated and then filtered. The filtrate was concentrated, diluted with pet. ether (B.P., 60-70°C) and subjected to chromatography on silicic acid. The column was eluted successively with pet. ether (B.P., 60-70°C), pet. ether/benzene (1/1), benzene and finally benzene/methanol (90/10). The fraction containing farnesyl acetone eluted with benzene.

b. The smoke condensate in diethyl ether was washed with equal volumes of water 20 times (the water was saturated with sodium chloride and equilibrated with diethyl ether prior to washing). The diethyl ether was then removed (at subambient temperatures) and the concentrate was diluted with pet. ether (B.P. 60-70°C). This solution was chromatographed according to the procedure described in a.

Gas Chromatographic Conditions: The chromatogram in Figure 1 was obtained on Wilkens A-350 Aerograph* instrument equipped with a dual thermal conductivity detector. The column was 5' x 1/4" stainless steel packed with 18% SE-30 coated on Chromosorb/W (60-80 mesh, DMCS treated). The column oven temperature was programmed from 100°C to 260°C at 6° per min.; the injector and detector temperatures were maintained at 260°C throughout the run.

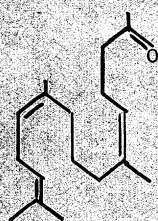
The collected eluate was purified by gas rechromatography on a Wilkens Aerograph 1520 under the following conditions: column, 5' x 1/4" stainless steel tubing packed with 20% FFAP coated on acid washed Chromosorb/W (60-80 mesh, DMCS treated); column oven temperature, programmed from 100°-205° at 4° per min., injector and detector temperature, 230°C.

The NMR spectrum of I was taken in deuterated chloroform on a Varian DP-60 spectrometer. Mass spectral studies were made on a CEC-103C instrument. Infrared spectra were obtained on the neat liquid in all cases, the instrument was a Beckman IR-7. Ultraviolet spectra were obtained on isooctane solutions, the instrument was a Cary Model 14.

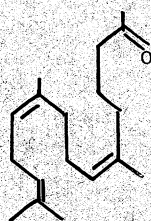
Acknowledgments

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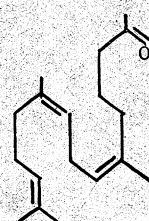
*Mention of a commercial item does not constitute endorsement of the United States Department of Agriculture over other items of a similar nature not mentioned.



IV



V



VI

seemed to be the most reasonable since it can be derived from solanescap (a known constituent of tobacco).

trated and then diluted with methanol. The methanol solution was allowed to stand overnight in the

Literature Cited

1. Bhati, A. Neophytadiene, the diterpenic hydrocarbon from tobacco, *Nicotiana tabacum* Hicks. *Perfumery Essent. Oil Record* 53: 685-688. 1962.
2. Cook, L. C. and A. Rodgman. The composition of cigarette smoke. XIV. Hexahydrofarnesyl acetone (phytone) and 2-methyl-5-isopropyl-1,3-nonadien-8-one (solanone) from Turkish tobacco smoke. *Tob. Sci.* IX: 137-139. 1965.
3. Isler, O., R. Rüegg, L. H. Chopard-dit-Jean, A. Winterstein and O. Wiss. Synthese und Isolierung von Vitamin K₂ und isoprenologen Verbindungen. *Helv. Chim. Acta.* 41:786-807. 1958.
4. Johnson, R. R. and J. A. Nicholson. The structure, chemistry, and synthesis of solanone. A new anomalous terpenoid ketone from tobacco. *J. Org. Chem.* 30:2918-2921. 1965.
5. Nazarov, I. N., B. P. Gussev and V. I. Gunar. Acetylene derivatives. CXCHII. Total synthesis of isoprenoid alcohols (linalool, geraniol, nerol, nerolidol, farnesol, geranyl-linalool, geranylgeraniol and phytol). *Zhur. Obshchei Khim.* 28: 1444-1458. 1958. (C.A., 53,1103g)
6. Ogg, C. L. and F. J. Cooper. Determination of unsaturation by microhydrogenation. *Anal. Chem.* 21:1400-1402. 1949.
7. Osman, S. and J. Barson. Hydrocinnamyl nitrile in cigar smoke condensate. *Chem. & Ind.* 17:699. 1966.
8. Osman, S., J. Barson and C. J. Dooley. Paraffins of cigar smoke. *J. Assoc. Offic. Agr. Chemists* 48: 1059-1062. 1965.



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